

REMARKS

This amendment and Remarks are filed in response to the Final Office action dated October 15, 2008.

Claim Objections

Claims 41-46 are objected to because of the following informalities: the claims are identified as ("new") but should be identified as "(previously presented)" since the claims were new in the previous amendment of 11/5/07. Appropriate correction is required.

Applicants apologize for obvious oversight and made appropriate corrections.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claim 38, step h), the specification fails to recite and support "growth and maturing of said chondrocytes or stem cells",

"integration of said construct seeded with said chondrocytes or stem cells into a native cartilage", and "both degraded within said three months" (last line).

Maturing of chondrocytes or stem cells is not described. The growth and maturing of cartilage occurs (paragraph 0110 of published specification). The specification fails to describe seeding of the construct and integration of the seeded construct into native cartilage. The specification describes seeding of the support matrix and integration of new cartilage into native cartilage (paragraphs 0031, 0110 and 0354). Description is not found of both the support matrix and polyethylene glycol cross-linked with methylated collagen degrading within three months. The specification describes the TRGH subsequently degrading after neo-cartilage is integrated into existing cartilage (paragraph 0173). Integration of the neo-cartilage would occur within three months since overgrowth of superficial cartilage occurs in about two-three months (paragraph 0110). While paragraph 0110 recites "about two-three months when the sealant is itself degraded", this means the sealant is degraded after the two-three months since paragraph 0173 discloses TRGH subsequently degrading after the integration of the neo-cartilage.

Applicants disagree. However, in order to advance the prosecution, Applicants amended claims to cancel the "growth and maturing of said chondrocytes or stem cells" language; changed the "integration of said construct seeded with said chondrocytes or stem cells into a native cartilage" language into "integration of said construct" that is supported in the specification, and canceled the language concerning the degradation.

"Integration of said construct" is supported in the specification as follows. The neo-cartilage construct as being integrated into the native cartilage is described as such in the Definitions, in line 1 and lines 5-6 of [0110]. The neo-cartilage construct is further described in lines 10-12 of [0111], as "the neo-cartilage construct introduced into the lesion is integrated into the native cartilage surrounding the cavity..." and in lines 8-10 in [0199] as "integration of neo-cartilage implanted into the lesion as the neo-cartilage construct". Applicants previously used the term neo-cartilage but Examiner objected to its use as indefinite. Should Examiner maintain that the term "construct" is not supported, Applicants would be willing to change the "construct" to "neo-cartilage construct", that is quite clearly supported in several places in the specification.

The term construct as being integrated into the native cartilage is fully supported and the rejection should be withdrawn.

Examiner further argues that support is not found in the specification for the superficial cartilage layer constituting a substitute synovial membrane as required in claim 47 when the superficial cartilage layer is a layer of squamous-like flattened superficial zone chondrocytes covering as required in claim 38 (lines 12-14 of step h). The specification is unclear as to the relationship of the substitute synovial membrane to the layer of squamous-like flattened superficial zone chondrocytes covering. The specification fails to describe how the two superficial cartilage layers relate to each other. Are the two superficial

cartilage layers alternative layers or is one layer a species of the other layer or are both layers inherently the same?

Applicants disagree with Examiner that the superficial cartilage layer constituting a substitute synovial membrane as required in claim 47 is not supported. Such support is found in paragraph [0349]. This paragraph discloses that "The deposition of the second top sealant layer resulting in formation of superficial cartilage layer constitutes **a substitute for synovial membrane** and provides the outer surface of healthy articular cartilage overgrowing, protecting, containing and providing critical metabolic factors aiding in growth and incorporation of autologous neo-cartilage in the lesion".

Thus when the second sealant, namely polyethylene glycol-methylated collagen is deposited over the implanted neo-cartilage construct, it results in formation of the superficial cartilage layer that looks like and functions like a healthy synovial membrane of the uninjured joint.

The term substitute synovial membrane is supported in the specification. Rejection should be withdrawn.

Examiner further argues that support is not found for the superficial cartilage layer as a layer of squamous-like flattened superficial zone chondrocytes covering as required in claim 38 (lines 12-14 of step h). The specification is unclear as to the relationship of the substitute synovial membrane to the layer of squamous-like flattened superficial zone chondrocytes covering. The specification fails to describe how the two superficial cartilage layers relate to each other. Are the two superficial cartilage layers alternative layers or is one layer a species of the other layer or are both layers inherently the same?

Again, Applicants disagree. Step h) of claim 38 requires that the neo-cartilage construct seeded with chondrocytes or stem cells is implanted into the cartilage lesion and polyethylene glycol cross-linked with methylated collagen is deposited over the implanted construct. Both these events result, in three months, in integration of the construct into a native cartilage and in the development of the superficial cartilage layer over the polyethylene glycol-methylated collagen. The superficial cartilage layer overgrows, that is, it grows over, the polyethylene glycol-methylated collagen and over the construct implanted in the lesion under the layer of polyethylene glycol-methylated collagen. Thus, during the injury the normal healthy joint cartilage covered with a native uninjured synovial membrane is broken and the lesion as well as a break in the covering synovial membrane appears. As a result of the injury and at a time of implantation, therefore, the joint cartilage has a lesion and the native synovial membrane that normally covers the joint cartilage is broken and disturbed. After the implantation of the construct into the lesion and after the deposition of polyethylene glycol-methylated collagen over the implanted construct, with time, the superficial cartilage layer begins to form. This superficial cartilage layer contains flattened chondrocytes that look like a squamous cells. All this is disclosed in the specification. However, to make the claims clearer and more definite, these terms were canceled from the claims.

Claims 38-47 are fully supported in the specification, as indicated. It is requested that Examiner withdraw his rejection and let the claims pass to issue.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Examiner argues that in line 6 of step f) of claim 38, reciting "chondrocytes" is confusing since the claim previously recites "chondrocytes or stem cells". It is suggested "chondrocytes" be changed to --- said chondrocytes or stem cells --- to be consistent with the previous recitation and be clear that the chondrocytes or stem cells are those previously required.

Applicants disagree. However, to advance prosecution, Applicants amended claims as suggested by the Examiner.

Examiner argues that bridging lines 6 and 7 of step h), "maturing of said chondrocytes or stem cells" is unclear as to physical phenomena that constitutes maturing of said chondrocytes or stem cells. How maturing differs from growth of the cells is uncertain.

Applicants disagree. However, in order to meet Examiner's rejections, Applicants canceled the "in growth and maturing said chondrocytes or stem cells" language from the claims.

Examiner argues that bridging lines 7 and 8 of step h), "said construct seeded with said chondrocytes or stem cells" does not have clear antecedent basis. In previous step e), the support matrix is seeded, and in step f) the seeded support matrix is subjected to conditions to produce the construct.

Applicants disagree. However to advance the examination Applicants canceled the language "seeded with said chondrocytes or stem cells".

Examiner argues that bridging lines 7 and 8 of step h), "integration of said construct" is confusing since the specification discloses new cartilage integrating, and not the construct integrating.

Applicants disagree that the language is confusing. Although fully defined, Examiner previously rejected the use of the term "neo-cartilage" that is the "new" cartilage as being indefinite for not being clear what is "new" cartilage and what is not "new" cartilage. Applicants then canceled that term from the claims. Now Examiner comes back and rejects the term "construct" because the specification describes integration of the new cartilage (neo-cartilage) construct.

Applicants respectfully submit that the neo-cartilage construct as being integrated into the native cartilage is described as such in the Definitions, in line 1 and lines 5-6 of [0110] as neo-cartilage construct. The neo-cartilage construct is further described in lines 10-12 of [0111], "the neo-cartilage construct introduced into the lesion is integrated into the

native cartilage surrounding the cavity..." and in lines 8-10 in [0199] as "integration of neo-cartilage implanted into the lesion as the neo-cartilage construct".

The term construct as being integrated into the native cartilage is fully supported and the rejection should be withdrawn. However, to make the claim 38 even more definite, Applicants amended the claims to require that implanting said construct within the lesion results in integration of the construct into the native cartilage, as supported in [0110], lines 10-12. Should Examiner agree, Applicants would be willing to amend claims to "neo-cartilage construct" rather than "construct".

Examiner further reject claim 38 as indefinite and confusing because bridging lines 10 and 11 of step h), requiring a superficial cartilage layer to overgrow the construct is confusing since polyethylene glycol cross-linked with methylated collagen has been deposited over the construct in lines 1-2 of step h). Therefore, the superficial cartilage layer should be required to overgrow the polyethylene glycol cross-linked with methylated collagen deposited over the construct.

Again, Applicants disagree. As stated in [0110], lines 10-14 "The top sealant layer promotes an overgrowth of the lesion with the superficial cartilage layer typically in about two-three months when the sealant is itself **degraded**." The lines Examiner found confusing are limited to "within three months". Additionally, [0275], lines 15-16 state "the second sealant is an initiator or substrate for the formation of a superficial cartilage layer."



Applicants point out to the Examiner that the last paragraph of claim 38 makes it clear that within three months both the support matrix of the construct and the PEG-methylated collagen are biodegraded, thus making the language of lines 10-11 definite. However, in an effort to arrive at the allowable set of claims, Applicants canceled the last paragraph of step h) from claim 38.

In line 13 of step h), "squamous-like" is uncertain as to meaning and scope. Being "like" squamous is relative and subjective, and depends on individual interpretation of how similar to squamous is like squamous.

Applicants disagree, however, to advance the examination, Applicants canceled the term "squamous-like".

Examiner also find, in line 14 of step h), "flattened superficial zone chondrocytes covering a layer" language unclear as to meaning and scope. The relationship of the chondrocytes to the flattened superficial zone, and the material flattened is unclear. Are the chondrocytes, the zone or both flattened? How a zone can be flattened is uncertain since a zone is not a physical material? Additionally, "flattened superficial zone chondrocytes" is confusing since the claim previously recites "said chondrocytes or stem cells", and relationship of the flattened superficial zone chondrocytes to the chondrocytes or stem cells previously required is unclear.

Bridging lines 12 and 13 of step h), "cartilage layer is an outermost layer" is unclear how this further defines the cartilage layer in addition to forming a superficial cartilage layer that overgrows the construct as required in lines 9-11. If

the superficial cartilage layer overgrows the construct, the superficial cartilage layer is inherently an outermost layer.

Applicants disagree. Both above rejections are clearly described and terms defined in the specification. [0088] describes "Superficial cartilage layer" as an outermost layer of cartilage that forms the layer of squamous-like flattened superficial zone chondrocytes covering the layer of the second sealant and overgrowing the lesion. [0098] describes "Superficial zone cartilage" as the flattened outermost layer of chondrocytes covering the extracellular matrix intermediate zone and deeper zone of mature articular cartilage in which non-dividing cells are dispersed.

Quite clearly immature activated chondrocytes of the construct and flattened chondrocytes of the superficial cartilage layer are not the same chondrocytes. Deposition of the PEG-methylated collagen over the construct induces the overgrowth of the lesion, that was implanted with the neo-cartilage construct and covered with PEG-methylated collagen, with the superficial cartilage layer that is formed of the layer of squamous-like flattened chondrocytes. As stated in [0349], "The deposition of the second top sealant layer resulting in formation of superficial cartilage layer **constitutes a substitute for synovial membrane** and provides the outer surface of healthy articular cartilage overgrowing, protecting, containing and providing critical metabolic factors aiding in growth and incorporation of autologous neo-cartilage in the lesion. However, Applicants amended claim 38, step h) to further clarify this point.

In lines 17-19 of step h), requiring the support matrix and polyethylene glycol cross-linked with methylated collagen to both

degrade in three months is confusing since lines 6-9 require integration of the seeded construct into native cartilage within three months. The polymer matrix forms the construct, and if both the support matrix and sealant (polyethylene glycol cross-linked with methylated collagen) degrade within three months, there will be no construct to undergo integration within three months. Additionally, if the sealant degrades within three months, there will be no sealant for the superficial cartilage layer to overgrow within three months as required in lines 6-11. It is suggested the added portion by amendment to step h) from "a" in line 6 to "in" in line 9, and lines 12-19 be deleted.

Applicants disagree, however, in an effort to expedite the prosecution, Applicants amended claims as suggested.

With these amendments, it is believed that the language of claim 38 is clear and definite and the rejection should be withdrawn.

Claim 47 is unclear as to the relationship of the superficial cartilage layer that constitutes a substitute synovial membrane to the superficial cartilage layer that forms a layer of squamous-like flattened superficial zone chondrocytes in line 13-14 of step h). How these two superficial cartilage layers differ and relate to each other is unclear.

Examiner further suggest that in line 2 of claim 47, --- forming --- should be inserted after "constitutes" to be consistent with "formation" previously recited.

Applicants amended claim 47 as suggested. Responding to Examiners argument regarding claim 47, as explained above, the superficial cartilage layer is a layer that forms over the implanted construct and over the PEG-methylated collagen and thus

over the treated lesion. When there is injury resulting in the cartilage lesion, the healthy synovial membrane is broken and the lesion is exposed to the outer environment. By providing the implant and means for formation of the superficial cartilage layer, such formed superficial cartilage layer functions as a substitute for the healthy uninjured synovial membrane.

All rejection under 35 USC 112, second paragraph have been overcome with amendments or with submitted arguments. With all rejection being addressed and overcome, it is submitted that all claims are in conditions for allowance. Examiner is respectfully requested to withdraw the rejections and allow the claims.

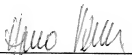
Applicants appreciate Examiner's finding that the claims are free of the prior art.

SUMMARY

In summary, claims 38-47 are amended, arguments are provided to overcome rejections under 35 USC112, first and second paragraph. It is believed that all claims are in conditions for allowance. Notice of allowance is respectfully requested.

Respectfully submitted,

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